**WP4 – NIHE: Comparative study of AMR in pig famers**

1.

Vietnam has recorded several cases of foodborne zoonotic diseases (FBZ), especially pig-related illness. In Vietnam, pigs are of paramount importance due to their benefaction to human sustenance, their commission in agronomic production structures, and their economic engagement. However, studies on these diseases in this country remain limited. Recently, FBZs are human infections transmitted through ingested food and caused by pathogens which natural reservoir is a vertebrate animal species (Hubalek [2003](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR55)). In Vietnam, suspected outbreaks of foodborne disease are reported to the Vietnam Food Administration (VFA) (<http://vfa.gov.vn>). In 2011, 148 outbreaks were reported, with 38,915 cases, 3,663 hospitalizations and 27 deaths. In most cases, FBZ aetiologies remain undetermined, and the relative disease burden compared to other infectious diseases cannot be readily quantified.

There is a list of the most important bacterial pathogens that caused human FBZ in Vietnam

***E. coli***

*E. coli* is a commensal bacteria in the gut of human and warm-blooded animal. However, some of them are common pathogens that cause not only intestinal infection but also extra-intestinal infectious disease in human. Numerous studies has been conducted in Extended-spectrum beta-lactamase-producing *E. coli* isolated from food, patients and livestock.

***Staphylococcus aureus***

*Staphylococcal* food poisoning is a gastrointestinal illness caused by eating food contaminated with toxins produced by the bacterium *Staphylococcus aureus* bacteria.

A recent study on Staphylococcus aureus isolated from blood showed 19% were methicillin resistant (n = 80) [[30](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4116647/#B30)]. National surveillance of community and hospital acquired infections (HAIs) show methicillin resistance rates up to 40% [[17](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4116647/#B17)].

Methicillin-resistant Staphylococcus aureus (MRSA) has been proposed to be common among health facilities in Asia, but recent data on MRSA prevalence in Southeast Asia is limited (84). In the community, recent studies reported a 7.9% prevalence of MRSA carriage in the rural and urban population in Vietnam (85)

***Non typhoidal salmonella (NTS)***

NTS prevalence in various farm animals (pre-slaughter) and in slaughter and retail facilities is summarized. Detected levels in meat are high, suggesting widespread contamination during slaughtering/processing. NTS carriage has been detected in ~5% of healthy adults (personal communication).

The antimicrobial susceptibility profiles of NTS isolates in Vietnam

| **Antimicrobial susceptibility profile** | **Human blood isolates (*n*, %)** | **Human stool isolates (*n*, %)** | **Animal isolates (*n*, %)** |
| --- | --- | --- | --- |
| Total tested | 148 (100) | 211 (100) | 313 (100) |
| Fully susceptible | 28 (18.92) | 111 (52.61) | 167 (53.35) |
| R-Ampicillin | 98 (66.22) | 71 (33.65) | 72 (23) |
| R-Amikacin | 21 (14.19) | 21 (9.95) | 21 (6.71) |
| R-Ceftazidime | 2 (1.35) | 7 (3.32) | 3 (0.96) |
| R-Ceftriaxone | 4 (2.7) | 6 (2.84) | 3 (0.96) |
| R-Chloramphenicol | 59 (39.86) | 51 (24.17) | 71 (22.68) |
| R-Ciprofloxacin | 76 (51.35) | 17 (8.06) | 61 (19.49) |
| R-Gentamycin | 46 (31.08) | 27 (12.8) | 18 (5.75) |
| R-Trimethoprim-sulfamethoxazole | 58 (39.19) | 53 (25.12) | 72 (23) |
| R-Clinically important agent[a](https://www.sciencedirect.com/science/article/pii/S1567134820303658" \l "tf0010) | 120 (81.08) | 94 (44.55) | 136 (43.45) |
| MDR[b](https://www.sciencedirect.com/science/article/pii/S1567134820303658" \l "tf0015) | 61 (41.22) | 50 (23.7) | 1. 15.02) |

### ***Campylobacter* spp.**

Globally, *Campylobacter* is the single most common human bacterial diarrhoeal pathogen, and together with NTS, account for ~90% of foodborne bacterial disease. In Vietnam, as in other countries, *C. jejuni* is the dominant species found in paediatric clinical cases (~85%) (Isenbarger et al. [2001](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR63)), with the remainder due to *C. coli*. Reported *Campylobacter* prevalence in Vietnamese poultry meat ranges from 28 to 31% (Ha and Pham [2006](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR45); Luu et al. [2006](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR82)). A 2005–2006 investigation of *Campylobacter* spp. at slaughterpoints in five cities worldwide indicated lowest prevalence in Ho Chi Minh City (HCMC) (15.3%, vs. an overall prevalence of 65.5%); 74% were *C. lari*, 9% *C.* *coli*, 4% *C.* *jejuni*and 13% other species. Semi-industrial poultry slaughtering was associated with lower contamination than informal direct slaughter by sellers (Garin et al. [2012](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR41)). In Vietnam, there are no published data on pre-slaughter (on-farm) prevalence or *Campylobacter* species diversity.

The relative contribution of *Campylobacter* and NTS to diarrhoea is not particularly high, and asymptomatic infections appear to be common. Given the widespread prevalence of NTS and *Campylobacter* in food products, and the intense human–animal exposures for most rural Vietnamese, the low incidence of clinical disease may reflect high levels of population immunity.

### ***Listeria* spp.**

*Listeria monocytogenes* causes abortion and sepsis-like infection in humans, especially among immunocompromised individuals, neonates, pregnant women and the elderly. Clinical *L.* *monocytogenes* infection was confirmed in 2008–2009, among three patients with meningitis in Hanoi (Chau et al. [2010](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR12); Tran et al. [2010](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR13)). Listeriosis has been linked to consumption of unpasteurised soft cheeses, processed meat and fish products. A study of fish and seafood products from Nha Trang Bay (central Vietnam) identified *L. monocytogenes* in 5.8% (Beleneva [2011](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR6)).

There are no data on the prevalence of *L. monocytogenes* in meat products in Vietnam, but studies in the region (Thailand) suggest a high prevalence of *L. monocytogenes* in raw meats, especially in those sold in supermarkets (Indrawattana et al. [2011](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR62)). In Vietnam, meat is being increasingly purchased from supermarkets, especially in urban areas.

### ***Streptococcus suis***

In Vietnam, *Streptococcus suis*  is the leading cause of bacterial meningitis in adult humans. A case–control study identified the following risk factors: (1) eating undercooked pig blood/intestine; (2) occupation related to pigs; and (3) exposure to pigs while having skin injuries (Nghia et al. [2011](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR90)). Due to poorly regulated marketing systems, ill pigs may enter the food chain, thus posing a significant risk to both slaughterhouse workers and consumers. Consumption of pig blood, intestines and organ meats is common in Vietnam (Wertheim et al. [2009a](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR142). *Streptococcus suis* carriage rates of 41% (*n* = 542) have been identified in healthy Vietnamese pigs. Serotype 2 appears to be dominant (14%), followed by serotypes 3, 21, 21 and 16 (Ngo et al. [2011](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR91)). An increase in tetracycline (88.6%) and chloramphenicol (8.6%) resistance was observed in S. suis over an 11-year period, associated with agricultural antibiotic use [[29](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4116647/#B29)]. However, there is very limited data on antibiotic resistance strains in Vietnam.

### ***Leptospira* spp**

Leptospirosis is caused by several pathogenic species within the genus *Leptospira*. Humans become infected through cuts, skin abrasions or by drinking contaminated water. Symptoms can range from mild, influenza-like illness to severe infection with renal and hepatic failure, pulmonary distress and death (Adler and de la Pena Moctezuma [2010](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR1)).

Leptospiras have a broad range of animal reservoirs. Most studies in Vietnam have focused on pigs due to their impact on swine reproduction. In the Mekong Delta, Bratislava, Icterohaemorrhagiae, Automnalis, Grippotyphosa and Pomona are the most common serovars, with higher prevalence in small-scale farms compared to large holdings (Boqvist et al. [2002a](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR8), [b](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR9)). In general, there appears to be little overlap between serovars in pigs and humans; however, there is a paucity of surveillance data on which to judge exposures and epidemiological associations. The diffuse clinical picture and lack of straightforward diagnostics for leptospirosis (Wagenaar et al. [2004](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR140); Smythe et al. [2009](https://link.springer.com/article/10.1007/s10393-013-0884-9#ref-CR111)) hamper adequate case reporting from Vietnam.

\* Vietnam bears a heavy burden of infectious diseases and a high prevalence of antibiotic resistance due to inappropriate antibiotic use. Many studies have reported that antibiotics accounted for 50% of the drugs consumed in Vietnam and for 70% of pharmaceuticals used in livestock farmin. Especially in porcine and poultry productions, the overall annual consumption of in-feed antimicrobial agents has been estimated at 1,023 tons, of which 57% belonged to the WHO list of critically important antimicrobials for human medicines, including beta-lactams and colistin-one of the last resort drug. In addition, the food-animal processing facilities in Vietnam, especially the small-scale and non-intensive facilities, commonly locate close to populated community areas. Manual slaughtering with poor hygiene, missing biosecurity management and weak food safety control are also common weaknesses. These conditions exposed the community population to a higher risk of acquiring antibiotic resistance from food-animals.

**2. Compatative study of AMR in pigs farmers (The short initial description of background and work to be carried out in WP4)**

**2.1. Background WP4**

Vietnam bears a heavy burden of infectious diseases and a high prevalence of antibiotic resistance due to inappropriate antibiotic use. Antibiotics have been used in food-animal agriculture as therapeutic agents and growth promotions to increase the production and farrowing rates. As animal-associated and environment microbiomes can contribute to the spread of antibiotic resistance via local transmission among connected habitats, antibiotic resistance in food animal production can pose a significant risk to human health. Some characteristics of animal production and food consumption habits in Vietnam that may promote FBZ disease transmission include: (1) high density of both human and animal populations living in close proximity; (2) a predominance of smallholder production systems with mixed species and little/no biosecurity; (3) the presence of abattoirs and wet markets operating with rudimentary hygiene, limited cold chain for distribution and low levels of meat inspection; (3) widespread consumption of raw/undercooked blood, meat, organ tissues…, and (4) use of untreated wastewater and sewage for agriculture. Moreover, documented key drivers of resistance in human health settings are the use, overuse, misuse and irrational use of antimicrobials, particularly self-diagnosis and medication, over-prescription by medical practitioners, easy and/or illegal access to antimicrobial medication without a prescription and inadequate hygiene practices of health-care workers.

Vietnam is a potential hot spot for the emergence of AMR due to the high burden of infectious diseases that are directly transmissible and that are foodborne, coupled with limited enforcement of regulations to penalise non-compliance, and the relatively unregulated access to antimicrobials for humans and high antimicrobial usage for livestock

In addition, a lack of Point-of-care tests for diagnosis in primary healthcare could not help to reduce antibiotic overuse.

Pig farms……Xxxxx

**2.2. Methods**

***2.2.1. Sampling:***

Study sites: the pig farms will be identified by VOHUN and NIVR

In parallel, a type or number of samples will be determined by NIVR and NIHE team: e.g: feacal, urine or blood/farmers, family members….

**2.2.2. Laboratory analysis**

Screening and bacterial cultures

* Identification of pathogens by POC diagnostic device
* Bacterial cultures
* Antimicrobial susceptibility testing (AST) will be determined.
* The antibiotic resistant strains will be subjected to multilocus sequence typing (MLST) or NGS (if needed).

Storing

- The bacterial isolates will be stored in -70 °C for genetic follow-up studies.

**2.3. Expected outcomes**

* Evaluation of using POC diagnostic device in the primary healthcare in Vietnam
* Antibiotic resistance data of bacterial pathogens that isolated in farmers/and family members and comparison to animal strains (before/and after intervention?)
* Molecular epidemiologial data of human and animal strains; drug resistance…
  + The contamination of the slaughterhouse environment by food-animal originated plasmids, potential contamination of the slaughterhouse by plasmids originated from humans will be also observed.
  + A remarkably high prevalence of MDR strains in the human-animal-environment interface in Vietnam???